

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/051269

International filing date (day/month/year)
18.03.2005

Priority date (day/month/year)
22.03.2004

International Patent Classification (IPC) or both national classification and IPC
C07D471/04, A61K31/4745

Applicant
ALTANA PHARMA AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/051269

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/051269

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 13 (as regards industrial applicability)

because:

- ☒ the said international application, or the said claims Nos. 13 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/051269

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-13
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-13
Industrial applicability (IA)	Yes: Claims	1-12
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
 INTERNATIONAL SEARCHING
 AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2005/051269

Re Item III.

The present **claim 13** relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT.

Consequently, no opinion will be formulated with respect to industrial applicability of the subject-matter of this claim.

[For the assessment of the aforesaid claim on the question whether it is industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but will allow, however, claims to a (known) *compound for first use in medical treatment* and the *use of such a compound for the manufacture of a medicament for a new medical treatment*.]

Re Item V.

The following documents (D) are considered to be relevant:

D1: WO-A-03/014123 (20 February 2003);

D2: US-A-4468400 (28 August 1984);

D3: *Journal of Medicinal Chemistry* **40**(4), 427-436 (1997);

1. NOVELTY (Article 33(2) PCT):

The present application satisfies the criterion set forth in Article 33(2) PCT because the subject-matter of **claims 1-13** is new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT):

The compounds of the present independent **claim 1** differ from the compounds of the prior art **D1** (cf., claim 1 therein) in that they are 7,8,9,10-tetrahydro-imidazo[2,1-*a*]isoquinolines rather than 7*H*-8,9-dihydro-pyrano[2,3-*c*]imidazo[1,2-*a*]pyridines or 7,8,9,10-tetrahydro-imidazo[1,2-*h*][1,7]naphthiridines, respectively (cf., the definition of the group X (= -O- or -NH-) in claim 1 of **D1** and the corresponding present -CH₂- group).

They are further novel over the compounds of **D2** and **D3** (cf., claim 1 of **D2**; and the compounds of table 1 of **D3**) on account of the present substituent group **R3** (cf., the present 6-hydroxyalkyl and 6-carboxylic acid derivatives, the definition of the group X of **D2**, and the 6-unsubstituted derivatives of **D3**).

2. INVENTIVE STEP (Article 33(3) PCT):

The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of **claims 1-13** does not appear to involve an inventive step (Rule 65(1)(2) PCT):

Document **D1** - which represents the **closest prior art** - teaches (cf. claim 1 therein) i.a.

the *gastric acid secretion inhibitory* activity of some 7H-8,9-dihydro-pyrano[2,3-*c*]-imidazo[1,2-*a*]pyridine derivatives (see, for instance, the compound 2,3-Dimethyl-9-phenyl-7H-8,9-dihydro-pyrano[2,3-*c*]imidazo[1,2-*a*]pyridine-6-carboxylic acid dimethylamid of the example 3 on pages 13-14 of **D1**).

The correspondingly substituted derivative according to the present **claims 1-11** (see, the compound 2,3-Dimethyl-9-phenyl-7,8,9,10-tetrahydro-imidazo[2,1-*a*]isoquinoline-6-carboxylic acid dimethylamid of the present example 3) **differs** from the aforesaid **D1** compound essentially only in that it has a "central" 7,8,9,10-tetrahydro-imidazo[2,1-*a*]isoquinoline ring.

In the light of the prior art **D1** the **problem** to be solved by the present application has to be seen in the provision of further *gastric acid secretion inhibitors*.

This problem appears to be **solved** by the compounds of the present **claim 1** (cf., the table A on page 41 of the present description).

This solution cannot however be considered to involve an inventive step (Article 33(3) PCT) for the following reasons:

On consulting the prior art **D2** (cf., claim 1 therein; and, in particular, the correspondingly substituted compounds of column 3, lines 14-25 and column 3, line 39 - column 4, line 10), the person skilled in the art would have **known** that 9-phenyl-7H-8,9-dihydro-pyrano[2,3-*c*]imidazo[1,2-*a*]pyridine derivatives (cf., column 3, lines 14-25) **as well as** 9-phenyl-7,8,9,10-tetrahydro-imidazo[2,1-*a*]isoquinoline derivatives (cf., column 3, line 39 - column 4, line 10) possess *gastric acid secretion inhibitory* activity (cf., column 6, line 52).

Hence, he would have expected that the accordingly modified compounds of **D1** (cf., the compound of the example 3 of **D1** and the 2,3-Dimethyl-9-phenyl-7,8,9,10-tetrahydro-imidazo[2,1-*a*]isoquinoline-6-carboxylic acid dimethylamid of the present example 3)

would also display (some) *gastric acid secretion inhibitory* activity.

It is therefore considered that - in the absence of any **unexpected / surprising effect** - the present solution (i.e., the compounds of the present **claims 1-11**) has to be regarded to be **obvious** in the light of the prior art **D1** and **D2**.

Consequently, it is considered that the subject-matter of the present **claims 1-13** does **not** involve an inventive step as set forth in Article 33(3) PCT.

3. INDUSTRIAL APPLICABILITY (Article 33(4) PCT):

The subject-matter of the present **claims 1-12** concerns chemical compounds and a pharmaceutical composition and is therefore considered to be industrial applicable in the sense of Article 33(4) PCT.